(FILE 'HOME' ENTERED AT 14:56:47 ON 30 MAY 2003)

FILE 'MEDLINE' ENTERED AT 14:56:55 ON 30 MAY 2003

L1 0 S HBV AND (CHIMERIC OR CHIMERA)AND RGD

L2 0 S HBV AND RGD

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4/7/12
DIALOG(R)File 155:MEDLINE(R)


11598239 99030876 PMID: 9811704

An adenovirus vector with genetically modified fibers demonstrates expanded tropism via utilization of a coxsackievirus and adenovirus receptor-independent cell entry mechanism.

Dmitriev I; Krasnykh V; Miller C R; Wang M; Kashentseva E; Mikheeva G; Belousova N; Curiel D T

Gene Therapy Program, Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, Alabama 35294-3300, USA.

Journal of virology (UNITED STATES) Dec 1998, 72 (12) p9706-13, ISSN 0022-538X Journal Code: 0113724

Contract/Grant No.: CA-68245; CA; NCI; RO1 CA-74242; CA; NCI; RO1 HL-50255; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Recombinant adenoviruses (Ad) have become the vector system of choice for a variety of gene therapy applications. However, the utility of Ad vectors is limited due to the low efficiency of Ad-mediated gene transfer to cells expressing marginal levels of the coxsackievirus and adenovirus receptor (CAR). In order to achieve CAR-independent gene transfer by Ad vectors in clinically important contexts, we proposed modification of viral tropism via genetic alterations to the viral fiber protein. We have shown that incorporation of an Arg-Gly-Asp (RGD)-containing peptide in the HI loop of the fiber knob domain results in the ability of the virus to utilize an alternative receptor during the cell entry process. We have also demonstrated that due to its expanded tissue tropism, this novel vector is capable of efficient transduction of primary tumor cells. An increase in gene transfer to ovarian cancer cells of 2 to 3 orders of magnitude was demonstrated by the vector, suggesting that recombinant Ad containing fibers with an incorporated RGD peptide may be of great utility for treatment of neoplasms characterized by deficiency of the primary Ad type 5 receptor.

Record Date Created: 19981130

Record Date Completed: 19981

8/7/2
DIALOG(R)File 155:MEDLINE(R)


10530929 96342124 PMID: 8750015
Targeting of adenovirus penton base to new receptors through replacement of its RGD motif with other receptor-specific peptide motifs.
Wickham T J; Carrion M E; Kovesdi I
GenVec Inc, Rockville, MD 20852, USA.
Gene therapy (ENGLAND) Dec 1995, 2 (10) p750-6, ISSN 0969-7128
Journal Code: 9421525
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The adenovirus coat protein, penton base, contains the peptide motif RGD which mediates binding to the integrin cell surface receptors alpha v beta 3 and alpha v beta 5. These integrins then mediate adenovirus internalization. We have developed penton base chimeras that recognize tissue-specific integrin receptors by replacing the wild-type RGD peptide motif with alpha v beta 3- or alpha 4 beta 1-specific peptide motifs. In one chimera the original haiRGDtfa motif was replaced with the peptide motif eiLDVpst which mediated chimera binding to the integrin alpha 4 beta 1. This integrin is expressed at high levels on lymphocytes and monocytes but is not expressed on epithelial or endothelial cells. In a second chimera the wild-type sequences flanking the RGD motif were altered to abrogate its interaction with alpha v beta 5 while retaining its specificity for alpha v beta 3. The integrin alpha v beta 5 is expressed primarily on epithelial cells whereas the integrin alpha v beta 3 is normally expressed on endothelial cells. The integrin alpha v beta 3 is also aberrantly expressed on certain metastatic melanomas and glioblastomas. A deletion mutant lacking the RGD sequence did not bind to any integrins. Such chimeras incorporated into adenovirus virions may be useful in targeting specific tissues in adenovirus-mediated gene delivery.
Record Date Created: 19970325
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| Set | Items | Description |
|---|---|---|
| S1 | 24935 | ADENOVIR? |
| S2 | 70986 | FIBER OR FIBRE |
| S3 | 45605 | ENTRY |
| S4 | 54 | S1 AND S2 AND S3 |
| S5 | 814 | HEXON OR PENTON |
| S6 | 32122 | CHIMER? OR CHIMAER? |
| S7 | 31 | S1 AND S5 AND S6 |
| S8 | 2 | PENTON AND S7 |